



# Alzheimer's and the Gut Microbiome

It may not be surprising to learn that brain health is intricately linked to the state of the rest of the body. But what are the links, and what role do these connections play in diseases like Alzheimer's? Sam Sisodia, Ph.D., of the University of Chicago, is examining one of the most important connections: the way in which our gut microbiome influences the brain in Alzheimer's disease.

The "gut microbiome" refers to the population of microorganisms, mostly bacteria, that lives in every person's digestive tract. These are natural residents of our bodies, present even at birth. Each person's microbiome is different, containing more of certain microorganism species and less of others. Sisodia is exploring the makeup of the gut microbiome and its broader impact on our health.

Sisodia is working with mice bred to exhibit the hallmark traits of Alzheimer's disease: amyloid plaques, tau tangles, brain inflammation and loss of cognitive function. In a previous experiment, Sisodia treated some of these mice with antibiotics. As expected, these treated mice exhibited significant changes in their gut microbiomes. While overall bacteria levels remained the same, these mice had less bacterial diversity—certain species were no longer present, while others were present at elevated levels.

Sisodia was excited to see both fewer and smaller amyloid plaque depositions in the brains of treated mice. These mice showed higher levels of soluble amyloid beta and exhibited a different neuroinflammatory response from that of untreated mice. Inflammation in the brain is an immune response—an attempt by the body to fight an invading pathogen or to respond to other trauma—but it goes awry in Alzheimer's disease as microglial cells become overactive, causing damage to nerve cells.

The antibiotic-treated mice showed lower levels of these cells around the remaining plaques. Sisodia suspects that the change in this inflammatory response might be the reason for the differences in Alzheimer's pathology seen in the antibiotic-treated mice.

*continued on page 3 »*

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## INSIDE THIS REPORT

**\$50 Million in Research Funding**

2

**Dialogue with the National Institutes of Health on Alzheimer's Disease**

2

**Partnering for Cures**

3

**The Alzheimer's Piano—'Making Memories'**

3

**Our 6th Annual Symposium**

3

**Financial and Research Updates**

4

**Cure Alzheimer's Fund Heroes**

5

**One Family's Experience is a Lesson Learned for All**

6



# \$50 Million in Research Funding

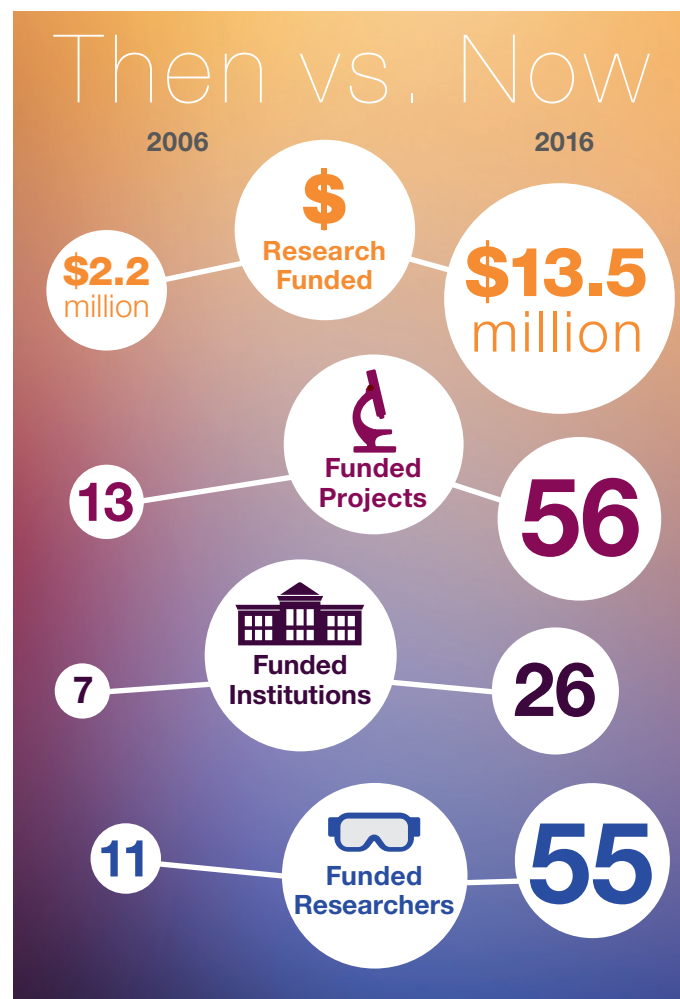
At the end of 2016 Cure Alzheimer's Fund hit a significant milestone: surpassing **\$50 million** in research funding since its inception 12 years ago. Growing awareness of the disease and the need for research has enabled us to gain momentum, fund more projects and get closer to a cure.

In 2016 alone, we allocated \$13.5 million in research, much greater than the \$10 million we funded in 2015. As a result, we were able to fund 56 projects at 26 separate institutions with 55 different scientists, 20 of whom were first-time recipients of Cure Alzheimer's Fund grants.

This growth also has allowed us to fund such larger-scale projects as CIRCUITS (Collaboration to Infer Regulatory Circuits and to Uncover Innovative Therapeutic Strategies), a new initiative with numerous grants to multiple scientists from different institutions based on a common theme. More of these multigrant, collaborative projects are planned, allowing researchers to dive deeper into important new areas of discovery and make quick progress.

For more information  
on CIRCUITS, visit  
[curealz.org/circuits](http://curealz.org/circuits)

This year promises to be another big year for research. The efforts of our generous and loyal donors have engendered this incredible growth and progress, and we thank you!



## Dialogue with the National Institutes of Health on Alzheimer's Disease

For the first time, Cure Alzheimer's Fund and the National Institutes of Health (NIH) joined forces to produce a live-streamed webinar titled "Dialogue with the National Institutes of Health on Alzheimer's Disease," which aired on Dec. 5, 2016, from NIH headquarters in Bethesda, Maryland. The webinar featured Dr. Richard J. Hodes, director of the National Institute on Aging (NIA), and Tim Armour, president and CEO of Cure Alzheimer's Fund, and was moderated by David Shenk, senior adviser to Cure Alzheimer's Fund.

As a division of NIH, the mission of the NIA is to improve the health and well-being of older people through biological, clinical, and social and behavioral research. The webinar provided a big-picture overview of the Alzheimer's disease research being conducted at NIH, how philanthropic organizations fit into the overall research picture, and how the public and private sectors are working together to fund innovative projects and bring them to scale. If you missed it, you can watch it online: <http://curealz.org/nih-webinar>.



Dr. Richard Hodes

L to R: NIA Director Dr. Richard Hodes, and Cure Alzheimer's Fund's David Shenk and Tim Armour.





## Partnering for Cures

In the world of medicine, collaboration is key. Individuals can learn from each other, share their progress and inspire new approaches to developing cures. That's the philosophy of FasterCures, Michael Milken's organization that sponsors Partnering for Cures, an annual conference that brings together hundreds of leaders from around the world to accelerate getting new therapies into the hands of patients.

This past November, patient advocates, researchers, investors and policy makers gathered in New York City to foster collaboration and advance medical

research. Individuals from Cure Alzheimer's Fund attended, with the goal of making new connections across different sectors and industries, and gaining valuable insights.



L to R: Cure Alzheimer's Fund Senior Vice President Sally Rosenfield, NIH Director Dr. Francis Collins and Cure Alzheimer's Fund Senior Vice President John Slattery.

## Alzheimer's and the Gut Microbiome

*continued from cover »*

With these findings, Sisodia wants to know more. He now is testing the same antibiotics on a different strain of Alzheimer's mice, making sure the effects he saw were not specific to the original mouse strain tested. He's also investigating *why* changes in the gut microbiome might affect immune responses in the brain. "It's fascinating to learn that what happens in our digestive tract can influence the pathology of Alzheimer's in our brains, but if this work is going to lead us closer to a cure, we need to understand the mechanisms of action," Sisodia said.

Sisodia's work promises to uncover new insights into the causes and risk factors of Alzheimer's disease, and hopefully identify targets for treatment. However, Sisodia strongly cautions against interpreting his work as a suggestion that antibiotics themselves might be a treatment for Alzheimer's.

"I am investigating how gut microbial diversity impacts Alzheimer's pathology, and antibiotics are a way to quickly alter that diversity in the lab—but my work does not support using antibiotics in human patients to address Alzheimer's," he said. "We need to learn more about the consequences of altering the gut microbiome, what an optimal microbiome population profile would be and how to achieve it. It's possible some changes might actually accelerate amyloid deposition in the brain. What's more, the overuse of antibiotics can have serious negative effects on the health of individuals and our population as a whole."

Sisodia's work also is deepening our understanding of one of the most critical components of Alzheimer's: inflammation. "While plaques and tangles are better known, inflammation is what most directly causes nerve cell death," he explained. "If we can figure out how to intervene in the processes that are responsible for the inflammation, we may be able to stop the disease from doing real damage to our brains."

*Dr. Sangram Sisodia was awarded a \$250,000 grant by Cure Alzheimer's Fund in 2016 for his project "Mechanisms By Which the Gut Microbiome Influences Amyloid Deposition and Neuroinflammation in Mouse Models of Alzheimer's Disease."*

## The Alzheimer's Piano—'Making Memories'

Last fall, "Play Me, I'm Yours," a public display featuring 60 pianos designed by local artists and placed in public spaces, returned to Boston. One of the pianos was designed by Newburyport, Massachusetts, artist Jeff Monahan. "Making Memories" featured large word graphics to show the connection between music and the brain. Monahan's wife, Barbara Chambers of Cure Alzheimer's Fund, said, "Music plays an important role in memory for those with Alzheimer's. People with advanced Alzheimer's who remember very little will remember music." With his piano, Monahan wanted to help educate people about the role music can play for those with Alzheimer's, and celebrate its importance in all of our lives. He dedicated the piano to all those suffering from Alzheimer's and helped raise awareness, one note at a time.

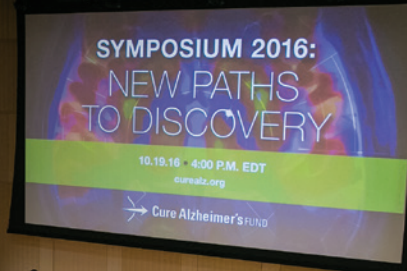
Jeff Monahan and the "Making Memories" Alzheimer's piano.



## Our 6th Annual Symposium

Thank you to those who attended or watched the live stream of our annual symposium in October and for supporting our cause! If you missed it, you can watch it online: <http://curealz.org/symposium>.

The 2017 symposium, "The Role of Infection in Alzheimer's Disease," will feature Drs. Rudy Tanzi and Rob Moir from Harvard University and Massachusetts General Hospital, and Dr. Sam Gandy from the Icahn School of Medicine at Mount Sinai. Be sure to mark your calendars for Thursday, Oct. 19, 2017, in Boston. You won't want to miss it!



*Hundreds of people came together for our 6th annual symposium.*

## Cure Alzheimer's FUND

34 Washington St.  
Suite 200  
Wellesley Hills, MA 02481  
p: 877-CURE-ALZ (287-3259)  
f: 781-658-2399  
[curealz.org](http://curealz.org)

Centre City Tower  
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Suite 2015  
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p: 412-261-2785

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Fund research  
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Contributing Writer: Patty Bovie  
Copy Editor: Colleen O'Neill  
Design: Winking Fish

## Financial Update

	This Quarter	YTD	Inception to Date
<b>Fundraising</b>	\$10.3M	\$15.7M	\$75.7M
<b>Expenses paid for by the board</b>	\$1.0M	\$3.1M	\$15.1M
<b>Funded research</b>	\$7.1M	\$13.5M	\$51.4M

Numbers shown are preliminary for the period and are rounded to the nearest \$100,000.

## Research Update (Research funded during the fourth quarter of 2016)

Project/Researcher	Distribution Amount
<b>Understanding Reactive Astrocytes and Their Roles in Alzheimer's Disease</b> – Ben A. Barres, M.D., Ph.D., Stanford University	\$150,000
<b>Cell Cycle Re-entry in 3-D Human Neuron Cultures</b> – John S. Lazo, Ph.D., and George S. Bloom, Ph.D., University of Virginia	\$100,000
<b>Amyloid Beta Expression Protects the Brain from Herpes Simplex Virus</b> – Robert Moir, Ph.D., Massachusetts General Hospital	\$175,000
<b>The Biological Impact of TREM Locus Mutations in Alzheimer's Disease</b> – Marco Colonna, M.D., and David Michael Holtzman, M.D., Washington University, St. Louis	\$250,000
<b>Characterization of Certain Human APOE Targeted Gene Replacement Mice</b> – David Michael Holtzman, M.D., and Jason D. Ulrich, Ph.D., Washington University, St. Louis	\$49,600
<b>Rejuvenation of Microglia in Brain Aging and Neurodegeneration</b> – Tony Wyss-Coray, Ph.D., Stanford University	\$150,000
<b>Alzheimer's Genome Project™</b> – Rudy Tanzi, Ph.D., Massachusetts General Hospital	\$1,500,000
<b>Studying the Functional Consequences of Alzheimer's Disease Risk Variants in the CLU and ABCA7 Genes Using Both Human and Mouse Models</b> – Li-Huei Tsai, Ph.D., Massachusetts Institute of Technology	\$250,000
<b>Extracellular Vesicle-Based Targeting of CD33-Mediated Pathology for Alzheimer's Disease Therapy</b> – Casey A. Maguire, Ph.D., Massachusetts General Hospital	\$150,000
<b>Systemic Inflammatory Networks in Alzheimer's Disease</b> – Filip Swirski, Ph.D., and Matthias Nahrendorf, M.D., Ph.D., Massachusetts General Hospital	\$200,000
<b>Identification of a Protective Human Immune Response for Alzheimer's Disease</b> – Charles Glabe, Ph.D., University of California, Irvine	\$125,000
<b>Regulation of Microglial Lysosome Acidification</b> – Frederick Maxfield, Ph.D., Weill Cornell Medical College	\$120,006
<b>Genes to Therapies™ (G2T) Centralized Research Core Oversight</b> – Wilma Wasco, Ph.D., Massachusetts General Hospital	\$173,750
<b>PICALM Gene Therapy and Drug Screening for Amyloid Beta Clearance</b> – Berislav Zlokovic, M.D., Ph.D., University of Southern California	\$225,000
<b>Discovery of CK1 Activators for Inducing the Autophagic Degradation of APP Beta-CTF</b> – Paul Greengard, Ph.D., The Rockefeller University	\$450,000
<b>The APOE Mimetic Therapeutic Peptide CN-105 Attenuates AD Pathology and Improves Functional Outcomes in a Murine Model of Alzheimer's Disease</b> – Daniel Laskowitz, M.D., M.H.S., Duke University	\$112,662
<b>Targeting Beneficial Innate Immunity in Alzheimer's by IRAK-M Deletion</b> – Terrence Town, Ph.D., University of Southern California	\$150,000
<b>Intersection of Microglial Transcriptomes to Identify Key Alzheimer's Pathways of Brain Phagocytes</b> – Sam Gandy, M.D., Ph.D., Icahn School of Medicine at Mount Sinai	\$150,000
<b>CIRCUITS: Utilizing Functional Maps to Prioritize Therapeutic Targets in Alzheimer's Disease</b> – Winston Hide, Ph.D., University of Sheffield	\$225,308
<b>CIRCUITS: Induced Pluripotent Stem Cells and the Human Brain</b> – Bradley T. Hyman, M.D., Ph.D., Massachusetts General Hospital	\$145,004
<b>CIRCUITS: Functional Analysis of Alzheimer's Disease Risk Genes Using Human-Induced Pluripotent Stem Cells</b> – Li-Huei Tsai, Ph.D., Massachusetts Institute of Technology, and Manolis Kellis, Ph.D., Broad Institute	\$400,000
<b>CIRCUITS: Production Center for Reference and Variation Gene-Regulatory Maps</b> – Manolis Kellis, Ph.D., Broad Institute, and Li-Huei Tsai, Ph.D., Massachusetts Institute of Technology	\$750,000
<b>CIRCUITS: Epigenetic Determinants of Human Cognitive Aging</b> – Lars Bertram, M.D., University of Lübeck	\$199,600
<b>CIRCUITS: Interpreting Alzheimer's Disease-Associated Genetic Variation at Enhancer Regions</b> – Andreas R. Pfenning, Ph.D., Carnegie Mellon University	\$189,610
<b>CIRCUITS: Whole Genome Characterization of DNA Methylation Changes in the Aged and Alzheimer's Disease Human Brain</b> – Rudolf Jaenisch, M.D., Whitehead Institute, and Joseph Ecker, Ph.D., Salk Institute	\$250,000
<b>G2T Research Models and Materials</b> – Taconic Biosciences	\$345,988
<b>Total Distributed to Research for Q4 2016</b>	<b>\$6,986,528</b>

Help us fund research with the highest probability of preventing, slowing or reversing Alzheimer's disease.  
Donations can be made through our website, [curealz.org/donate](http://curealz.org/donate), or sent directly to our office.

For gifts of securities or direct wire transfers, please contact Tim Armour  
at **877-CURE-ALZ (287-3259)** for further information.



*"Your donations make a big difference in our progress toward finding a cure for Alzheimer's disease. Your passion, your energy and your generosity are an inspiration to all of us to work even harder to end this terrible disease. Thank you all for your leadership and support."*

—Tim Armour, president and CEO, Cure Alzheimer's Fund

## A Daughter's Journey

Last November, Leslie McCabe, 46, of Fort Mill, South Carolina, ran the Novant Charlotte Marathon to raise money for Alzheimer's research and honor her mother, Bobbie Lonergan, who suffered from the disease before passing away four years ago. Leslie and her 12 siblings watched their mother slowly deteriorate. "We saw pieces of our mom disappear before our eyes, but she always kept her loving heart," said Leslie. Over the years, her sister Kerry

Luksic, author of *Life's Lessons from a Baker's Dozen*, which offers advice to caregivers and families of those afflicted, often was by Leslie's side. "Kerry and I ran many miles together during our mom's decline. Those were therapy sessions... It was such a difficult time, but we got through it," she said. "Running clears my head and puts everything in perspective." And it reminds Leslie that she's doing everything she can to fight the disease.



L to R: Leslie McCabe, her sister Christa Lonergan, Bobbie Lonergan and Kerry Luksic.

## One Couple's Level Best

"I'm trying to keep this ship afloat. I'm trying not to lose hope," are the opening lyrics to "Level Best," a song co-written by Mila Maring-Sims, caregiver for her husband Kelley, who was diagnosed with early-onset Alzheimer's disease in 2014. "As members of several bluegrass bands, my husband and I have been a part of the acoustic music scene in Southern Illinois since the 1980s," said

Mila. "As his condition progressed, we felt compelled to record a sort of bucket list album together, celebrating the many fine people we have come to know as a result of our musical endeavors"—and to help support Alzheimer's research. A portion of all proceeds from digital downloads of "Level Best" will go toward finding a cure. To download your copy, visit [www.cdbaby.com/cd/ruralking](http://www.cdbaby.com/cd/ruralking).



Kelley and Mila perform

Photo courtesy of Jen Haselhorst Photography

## END ALZ Pickleball Paddles

Neil Friedenberg, owner and president of ProLite Sports in Port Washington, Wisconsin, produces customized pickleball paddles for many different clients. When his wife's grandmother was diagnosed with Alzheimer's disease a few years ago, Neil said, "It took its toll on her very quickly and she later passed away. It was very difficult on all of us." In an

effort to raise awareness for the disease among pickleball players everywhere, ProLite designed and manufactured a limited-edition paddle with the words END ALZ on it. For each paddle sold, ProLite contributes \$15 to Cure Alzheimer's Fund. "Pickleball is a lifelong sport that bridges the gap between generations. We believe that more research is vital

to finding a cure for Alzheimer's, and this paddle is a tribute to the victims, friends and family who have suffered as a result of the disease," Neil said. To find out more, visit [ProLitePaddles.com](http://ProLitePaddles.com).

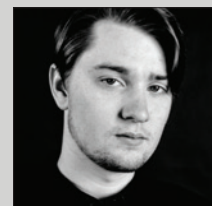


## Indie Filmmaker Gives Back

Joe Kowalski, 21, is a YouTuber, writer, actor and indie filmmaker from the Cleveland area. "Every time I make a film and have a local premiere, we give people the option to donate to a specific charity," explained Joe. This year he selected Cure Alzheimer's Fund. "I love the good work the organization does

and that 100 percent of donations goes directly to research. One of the characters in our newest film—"Prism"—has a form of dementia, so we thought it would be a nice tie-in," he said. "While Alzheimer's does not run in my family as far as I know, some of my closest friends and relatives' loved ones suffer from it."

Understandably, it's a cause he wanted to get behind. The premiere was held in November and 150 people attended. To find out more, visit [www.pogiejoe.com](http://www.pogiejoe.com).



Joe Kowalski



34 Washington St., Suite 200  
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## One Family's Experience is a Lesson Learned for All

Martha B. Capps of Raleigh, North Carolina, was a loving and caring mother to two children and a homemaker for most of her adult life. She also was a kind and trusting person. When Capps inherited a large sum of money from her aunt, she put her financial security in the hands of someone she thought to be trustworthy.

Her financial adviser, Hal Blondeau, promised to be ethically responsible and to act in her best interest. Despite his promise, Blondeau soon began siphoning millions of dollars from her to fund his own lavish lifestyle. When Capps was diagnosed with Alzheimer's disease in 2001, Blondeau took further advantage of her, capitalizing on a disease that robs those afflicted of their ability to make sound decisions.

Capps' son Bruce discovered some discrepancies and stepped in just in time. As the holder of his mother's power of attorney, he filed suit against Blondeau in 2007. After a seven-year legal battle, which Martha Capps would not live to see resolved, the Capps family ultimately was awarded more than \$10 million in damages. In addition, Blondeau was charged with investment adviser fraud and sent to prison.



*Martha B. Capps*

To honor their late mother's memory, Bruce and his sister, Carol Woodry, established the Martha B. Capps Family Foundation using funds awarded in their lawsuit against Blondeau. Over the years they have made significant annual financial contributions to Cure Alzheimer's Fund.

"It is emotionally trying when loved ones suffer with dementia, and even more horrible when others prey on their vulnerable state of mind," said Bruce. "It is our hope that the research community will soon cure Alzheimer's disease, thereby lessening the opportunities for fraudulent behavior by unscrupulous financial advisers and other service providers."